



Congenital hyperinsulinism in a newborn with a novel paternally inherited heterozygous mutation (p.E1517G) in the ABCC8 gene

Nancy Samir Elbarbary ¹, Sian Ellard ² & Khalid Hussain³

¹ Department of Pediatrics, Pediatric Diabetes and Endocrinology Unit, Faculty of Medicine, Ain Shams University, Cairo, Egypt ² Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Exeter Medical School, Exeter, United Kingdom ³ Department of Paediatric Endocrinology, Great Ormond Street Hospital for Children, London, UK

INTRODUCTION

- ❖ Congenital hyperinsulinism (CHI), a clinically and genetically heterogeneous disease, is the most common cause of persistent hypoglycemia in infancy.
- ❖ It is characterized by the unregulated secretion of insulin from pancreatic β -cells in relation to blood glucose concentration.
- ❖ The most common form of CHI is associated with autosomal recessive mutations in genes ABCC8 and KCNJ11, encoding the two subunits of the pancreatic β -cell ATP sensitive potassium channel (KATP).

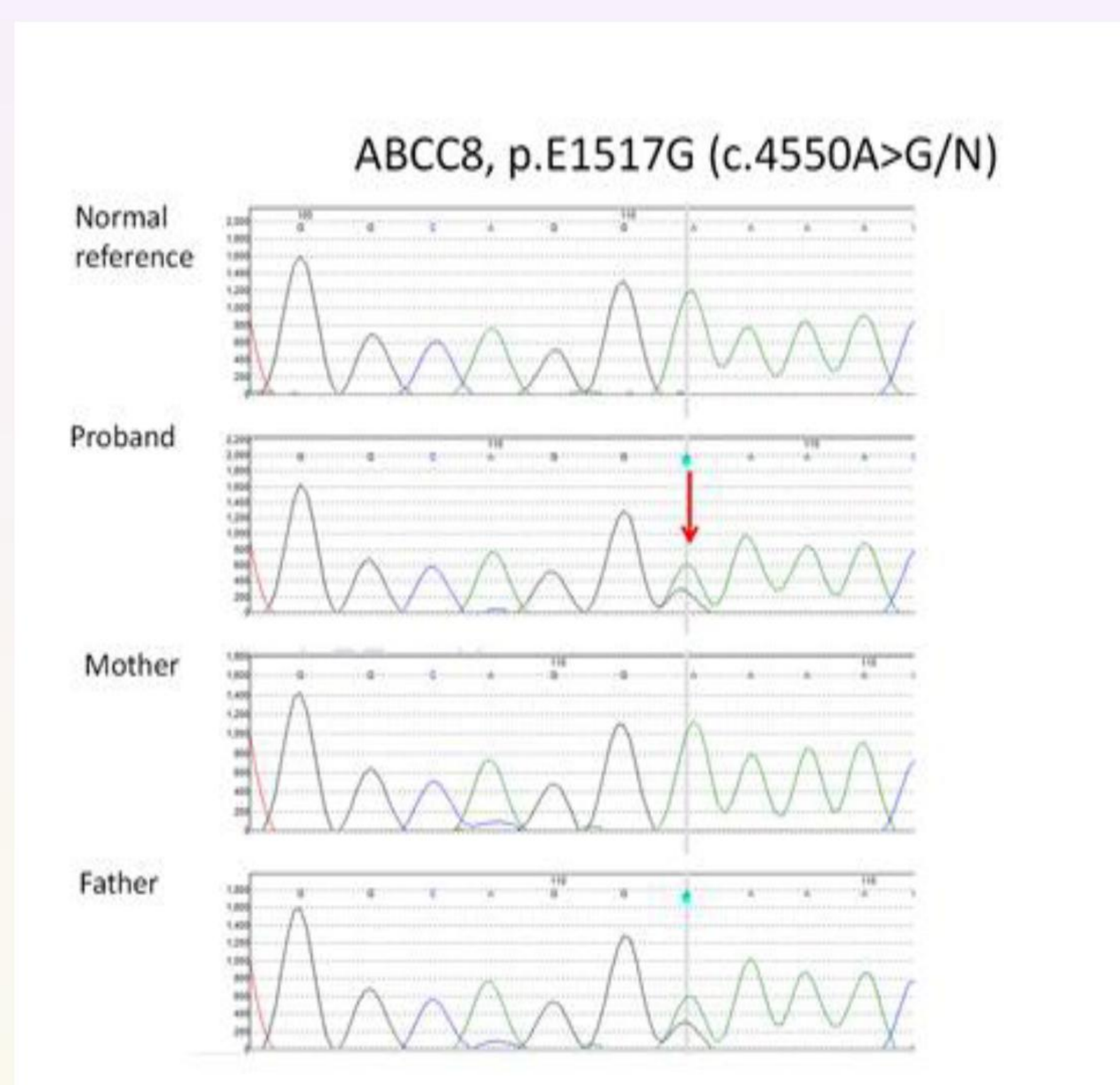
Case report

Here we describe an Egyptian male neonate first order of birth born to non consanguineous healthy parents. The pregnancy was uneventful and he was delivered at term vaginally . At day one of age he presented with severe hypoglycemia with generalized seizures. At the time of hypoglycemia (16 mg/dL) insulin and C-peptide levels were increased (insulin, 72uU/mL(6-25 uU/mL; C-peptide, 7.8 ng/mL(1.1-3.3 ng/mL), leading to the diagnosis of hyperinsulinism. Serum growth hormone, cortisol, ammonia and lactate were normal .On examination , the baby did not have any dysmorphic features or congenital anomalies. Patient was given glucose infusions and regular feeding every 2 h with increased amount of food was sufficient to maintain normoglycemia.

The patient was discharged and an out-patient follow-up was instituted without any treatment. However, recurrent episodes of hypoglycemia was noticed . Medications (Hydrocortisone and Nifedipine) had no substantial effect on glycemic profile. Another treatment was started on Diazoxide 10 mg/kg/day with increasing dosage up to 25 mg/ kg/day. This treatment was not effective and repeated episodes of hypoglycemia were observed 2–3 times a day. As parents refused surgery, Hydrochlorothiazide was added with substantial improvement of glycemic level. The child now is one year old growing well with no neurodevelopmental delay. Sequence analysis from the baby and both parents were taken and has identified a novel heterozygous missense mutation, p.E1517G (c.4550A>G) of the ABCC8 gene . Father Analysis of exon 38 of the ABCC8 gene showed heterozygous for the novel ABCC8 missense mutation. As the p.E1517G mutation has been paternally inherited a focal lesion is possible, no mutation was identified in the mother .

CONCLUSION

- ❖ Heterozygous paternally inherited ABCC8 mutations can lead to CHI which was responsive to medical treatment alone.



Figure(1): Sequence analysis from the baby and both parents were taken and has identified a novel heterozygous missense mutation, p.E1517G (c.4550A>G) of the ABCC8 gene



Figure(2): Photo of the indexed patient and both parents